

What is claimed is:

1. An isolated nucleic acid which encodes a polypeptide comprising the amino acid sequence shown in Figure 5 (Seq. I.D. No. 10) or a polypeptide having a sequence which varies therefrom by no more than 15 amino acids, such amino acid variations not involving amino acid positions 799-804 and not changing the functional properties of the polypeptide.
2. The nucleic acid of claim 1 encoding a polypeptide having the amino acid sequence shown in Figure 5 (Seq. I.D. No. 10).
3. The nucleic acid of claim 1, wherein the nucleic acid is DNA.
4. The DNA of claim 3, wherein the DNA is cDNA.
5. The DNA of claim 3, wherein the DNA is genomic DNA.
6. The nucleic acid of claim 1, wherein the nucleic acid is RNA.
7. A nucleic acid which comprises the nucleic acid of claim 1 linked to a nucleic acid encoding a flag epitope.
8. A nucleic acid which comprises the nucleic acid of claim 1 linked to a nucleic acid encoding a polypeptide corresponding to an artificial transmembrane region of a receptor which is not an Ob receptor.
9. A nucleic acid which comprises the nucleic acid of claim 8 linked to nucleic acid encoding a

09116676-071608

polypeptide corresponding to an artificial
intracellular domain of a receptor which is not an
Ob receptor

- 5 10. A purified polypeptide encoded by the nucleic acid
of claim 1, 2, or 7.
- 10 11. A purified polypeptide encoded by the nucleic acid
of claim 8.
12. A purified polypeptide encoded by the nucleic acid
of claim 9.
- 15 13. A vector comprising the nucleic acid of claim 1.
14. A vector of claim 13 adapted for expression in a
bacterial cell which comprises the regulatory
elements necessary for expression of the nucleic
acid in the bacterial cell operatively linked to the
20 nucleic acid encoding the polypeptide so as to
permit expression thereof.
15. A vector of claim 13 adapted for expression in a
yeast cell which comprises the regulatory elements
25 necessary for expression of the nucleic acid in the
yeast cell operatively linked to the nucleic acid
encoding the polypeptide so as to permit expression
thereof.
- 30 16. A vector of claim 13 adapted for expression in an
insect cell which comprises the regulatory elements
necessary for expression of the nucleic acid in the
insect cell operatively linked to the nucleic acid
encoding the polypeptide so as to permit expression
35 thereof.
17. A baculovirus vector of claim 16.

09116675, 071698

18. The baculovirus vector of claim 17 designated Bac-BO45 (ATCC Accession No. VR-2574).
19. A vector of claim 13 adapted for expression in an amphibian cell which comprises the regulatory elements necessary for expression of the nucleic acid in the amphibian cell operatively linked to the nucleic acid encoding the polypeptide so as to permit expression thereof.
20. A vector of claim 13 adapted for expression in a mammalian cell which comprises the regulatory elements necessary for expression of the nucleic acid in the mammalian cell operatively linked to the nucleic acid encoding the polypeptide so as to permit expression thereof.
21. A plasmid vector of claim 13.
22. A plasmid vector of claim 21 adapted for expression in a mammalian cell which comprises the regulatory elements necessary for expression of the nucleic acid in the mammalian cell operatively linked to the nucleic acid encoding the polypeptide so as to permit expression thereof.
23. The plasmid vector of claim 22 designated BO-25 (ATCC Accession No. 209036).
24. A vector comprising the nucleic acid of claim 8 or 9.
25. A vector of claim 24 adapted for expression in a bacterial cell which comprises the regulatory elements necessary for expression of the nucleic acid in the bacterial cell operatively linked to the nucleic acid encoding the polypeptide so as to

03116676-071698

permit expression thereof.

- 5 26. A vector of claim 24 adapted for expression in a yeast cell which comprises the regulatory elements necessary for expression of the nucleic acid in the yeast cell operatively linked to the nucleic acid encoding the polypeptide so as to permit expression thereof.
- 10 27. A vector of claim 24 adapted for expression in an insect cell which comprises the regulatory elements necessary for expression of the nucleic acid in the insect cell operatively linked to the nucleic acid encoding the polypeptide so as to permit expression thereof.
- 15 28. A baculovirus vector of claim 27.
- 20 29. A vector of claim 24 adapted for expression in an amphibian cell which comprises the regulatory elements necessary for expression of the nucleic acid in the amphibian cell operatively linked to the nucleic acid encoding the polypeptide so as to permit expression thereof.
- 25 30. A vector of claim 24 adapted for expression in a mammalian cell which comprises the regulatory elements necessary for expression of the nucleic acid in the mammalian cell operatively linked to the nucleic acid encoding the polypeptide so as to permit expression thereof.
- 30 31. A plasmid vector of claim 24.
- 35 32. A plasmid vector of claim 31 adapted for expression in a mammalian cell which comprises the regulatory elements necessary for expression of the nucleic

09116676.071698

acid in the mammalian cell operatively linked to the nucleic acid encoding the polypeptide so as to permit expression thereof.

- 5 33. A cell comprising the vector of claim 13.
34. A cell of claim 33, wherein the cell is a non-mammalian cell.
- 10 35. A cell of claim 34, wherein the non-mammalian cell is a *Xenopus* oocyte cell or a *Xenopus* melanophore cell.
- 15 36. A cell of claim 33, wherein the cell is a mammalian cell.
37. A mammalian cell of claim 36, wherein the cell is a COS-7 cell, a 293 human embryonic kidney cell, an NIH-3T3 cell, an LM(tk-) cell or a CHO cell.
- 20 38. An insect cell comprising the vector of claim 17.
39. An insect cell of claim 38, wherein the insect cell is an Sf9 cell, an Sf21 cell or a HighFive cell.
- 25 40. A cell comprising the vector of claim 24.
41. A cell of claim 40, wherein the cell is a non-mammalian cell.
- 30 42. A cell of claim 41, wherein the non-mammalian cell is a *Xenopus* oocyte cell or a *Xenopus* melanophore cell.
- 35 43. A cell of claim 40, wherein the cell is a mammalian cell.

09116676.071698

44. A mammalian cell of claim 43, wherein the cell is a COS-7 cell, a 293 human embryonic kidney cell, an NIH-3T3 cell, an LM(tk-) cell or a CHO cell.
- 5 45. An insect cell comprising the vector of claim 28.
46. An insect cell of claim 45, wherein the insect cell is an Sf9 cell, an Sf21 cell or a HighFive cell.
- 10 47. A membrane preparation isolated from the cell of claim 40.
48. A membrane preparation isolated from the cell of claim 45.
- 15 49. A nucleic acid probe comprising at least 15 nucleotides, which probe has a unique sequence corresponding to a sequence present within (a) the nucleic acid sequence from nucleotide number 2395 through nucleotide number 2412 of Figure 4 (Seq. I.D. No. 9) or (b) a reverse complement thereof.
- 20 50. The nucleic acid probe of claim 49, wherein the nucleotides are deoxyribonucleotides.
- 25 51. The nucleic acid probe of claim 49, wherein the nucleotides are ribonucleotides.
- 30 52. An antisense oligonucleotide having a unique sequence corresponding to a sequence present within (a) the nucleic acid sequence from nucleotide number 2395 through nucleotide number 2412 of Figure 4 (Seq. I.D. No. 9) or (b) a reverse complement thereof.
- 35 53. An antisense oligonucleotide of claim 52 capable of specifically hybridizing to mRNA, so as to prevent

09116676.071600

translation of mRNA.

54. An antisense oligonucleotide of claim 52 capable of specifically hybridizing to genomic DNA.

5

55. An antisense oligonucleotide of claim 52, wherein the oligonucleotide comprises chemically modified nucleotides or nucleotide analogues.

10

56. An antibody capable of specifically binding to the polypeptide containing at least a unique sequence corresponding to a sequence present within the amino acid sequence from amino acid number 799 through amino acid number 804 of Figure 5 (Seq. I.D. No. 10).

15

57. An antibody capable of competitively inhibiting the binding of the antibody of claim 56 to the polypeptide to which it specifically binds.

20

58. An antibody of claim 56, wherein the antibody is a monoclonal antibody.

25

59. A pharmaceutical composition comprising an amount of the oligonucleotide of claim 52 effective to reduce expression of a polypeptide and a pharmaceutically acceptable carrier.

30

60. A pharmaceutical composition of claim 59, wherein the oligonucleotide is coupled to a substance which inactivates mRNA.

35

61. A pharmaceutical composition of claim 60, wherein the substance which inactivates mRNA is a ribozyme.

62. A pharmaceutical composition of claim 61, wherein the pharmaceutically acceptable carrier comprises a

09116676-071698

structure which binds to a receptor on a cell capable of being taken up by the cells after binding to the structure.

- 5 63. A pharmaceutical composition of claim 62, wherein the pharmaceutically acceptable carrier is capable of binding to a receptor which is specific for a selected cell type.
- 10 64. A pharmaceutical composition which comprises an amount of the antibody of claim 56 effective to block binding of a ligand to the polypeptide and a pharmaceutically acceptable carrier.
- 15 65. A transgenic nonhuman mammal expressing a nucleic acid of any one of claims 1, 2, 7, 8 or 9.
66. A transgenic nonhuman mammal comprising a homologous recombination knockout of a polypeptide expressed by
20 a nucleic acid of any one of claims 1, 2, 7, 8 or 9.
67. A transgenic nonhuman mammal whose genome comprises antisense DNA complementary to a nucleic acid of any one of claims 1, 2, 7, 8 or 9 so placed as to be
25 transcribed into antisense mRNA which is complementary to mRNA encoding a polypeptide and which hybridizes to mRNA encoding a polypeptide, thereby reducing its translation.
- 30 68. The transgenic nonhuman mammal of claim 65, wherein the nucleic acid additionally comprises an inducible promoter.
69. The transgenic nonhuman mammal of claim 65, wherein
35 the nucleic acid additionally comprises tissue specific regulatory elements.

09116676, 071698

70. A transgenic ~~nonhuman~~ mammal of claim 65, wherein the transgenic ~~nonhuman~~ mammal is a mouse.

5
71. A process for identifying a chemical compound which specifically binds to a polypeptide of claim 10, which comprises contacting the polypeptide with the compound under conditions suitable for binding, and detecting specific binding of the chemical compound to the polypeptide.

10
72. The process of claim 71, wherein the specific binding of the compound to the polypeptide is detected by means of an antibody which binds to the polypeptide.

15
73. The process of claim 71, wherein the specific binding of the compound to the polypeptide is detected by a scintillation proximity assay.

20
74. The process of claim 71, wherein the polypeptide has substantially the same amino acid sequence as that shown in Figure 5.

25
75. The process of claim 71, wherein the compound is not previously known to bind to the polypeptide.

76. A compound determined by the process of claim 71.

30
77. A pharmaceutical composition which comprises an effective amount of a compound determined by the process of claim 71 and a pharmaceutically acceptable carrier.

35
78. A process involving competitive binding for identifying a chemical compound which specifically binds to a polypeptide of claim 10 which comprises separately contacting the polypeptide, with both the

09116676-071698

chemical compound and a second chemical compound known to bind to the polypeptide, and with only the second chemical compound, under conditions suitable for binding of both compounds, and detecting specific binding of the chemical compound to the polypeptide, a decrease in the binding of the second chemical compound to the polypeptide in the presence of the chemical compound indicating that the chemical compound binds to the polypeptide.

79. The process of claim 78, wherein the specific binding of the compound to the polypeptide is detected by means of an antibody which binds to the polypeptide.

80. The process of claim 78, wherein the specific binding of the compound to the polypeptide is detected by a scintillation proximity assay.

81. The process of claim 78, wherein the polypeptide has substantially the same amino acid sequence as that shown in Figure 5.

82. The process of claim 78, wherein the compound is not previously known to bind to the polypeptide.

83. A compound determined by the process of claim 78.

84. A pharmaceutical composition which comprises an effective amount of a compound determined by the process of claim 78 and a pharmaceutically acceptable carrier.

85. A process for identifying a chemical compound which specifically binds to a polypeptide encoded by a nucleic acid of claim 8 or 9, which comprises contacting cells containing DNA encoding and

09116676, 071698

expressing on the cell surface the polypeptide, with the compound under conditions suitable for binding, and detecting specific binding of the chemical compound to the polypeptide.

5

86. The process of claim 85, wherein the polypeptide has substantially the same amino acid sequence as that shown in Figure 5.

10

87. The process of claim 85, wherein the compound is not previously known to bind to the polypeptide.

88. A compound determined by the process of claim 85.

15

89. A pharmaceutical composition which comprises an effective amount of a compound determined by the process of claim 85 and a pharmaceutically acceptable carrier.

20

90. The process of claim 85, wherein the cell is an insect cell.

91. The process of claim 85, wherein the cell is a mammalian cell.

25

92. The process of claim 91, wherein the cell is nonneuronal in origin.

30

93. The process of claim 92, wherein the nonneuronal cell is a COS-7 cell, a 293 human embryonic kidney cell, an NIH-3T3 cell or an LM(tk-) cell.

35

94. A process for identifying a chemical compound which specifically binds to a polypeptide encoded by a nucleic acid of claim 8 or 9, which comprises contacting a membrane fraction from a cell extract of cells containing DNA encoding and expressing on

09116676.071698

their cell surface the polypeptide, with the compound under conditions suitable for binding, and detecting specific binding of the chemical compound to the polypeptide.

5

95. The process of claim 94, wherein the polypeptide has substantially the same amino acid sequence as that shown in Figure 5.

10

96. The process of claim 94, wherein the compound is not previously known to bind to the polypeptide.

97. A compound determined by the process of claim 94.

15

98. A pharmaceutical composition which comprises an effective amount of a compound determined by the process of claim 94 and a pharmaceutically acceptable carrier.

20

99. The process of claim 94, wherein the cell is an insect cell.

100. The process of claim 94, wherein the cell is a mammalian cell.

25

101. The process of claim 100, wherein the cell is nonneuronal in origin.

30

102. The process of 101, wherein the nonneuronal cell is a COS-7 cell, a 293 human embryonic kidney cell, an NIH-3T3 cell or an LM(tk-) cell.

35

103. A process involving competitive binding for identifying a chemical compound which specifically binds to a polypeptide encoded by a nucleic acid of claim 8 or 9, which comprises separately contacting cells expressing on their cell surface the

09116676.071698

polypeptide, with both the chemical compound and a second chemical compound known to bind to the polypeptide, and with only the second chemical compound, under conditions suitable for binding of both compounds, and detecting specific binding of the chemical compound to the polypeptide, a decrease in the binding of the second chemical compound to the polypeptide in the presence of the chemical compound indicating that the chemical compound binds to the polypeptide.

104. The process of claim 103, wherein the polypeptide has the amino acid sequence shown in Figure 5 (Seq. I.D. No. 10).

105. The process of claim 103, wherein the cell is an insect cell.

106. The process of claim 103, wherein the cell is a mammalian cell.

107. The process of claim 106, wherein the cell is nonneuronal in origin.

108. The process of claim 107, wherein the nonneuronal cell is a COS-7 cell, a 293 human embryonic kidney cell, an NIH-3T3 cell or an LM(tk-) cell.

109. The process of claim 103, wherein the compound is not previously known to bind to the polypeptide.

110. A compound determined by the process of claim 103.

111. A pharmaceutical composition which comprises an effective amount of a compound determined by the process of claim 103 and a pharmaceutically acceptable carrier.

09115576, 071698

112. A process involving competitive binding for identifying a chemical compound which specifically binds to a polypeptide encoded by a nucleic acid of claim 8 or 9, which comprises separately contacting a membrane fraction from a cell extract of cells expressing on their cell surface the polypeptide, with both the chemical compound and a second chemical compound known to bind to the polypeptide, and with only the second chemical compound, under conditions suitable for binding of both compounds, and detecting specific binding of the chemical compound to the polypeptide, a decrease in the binding of the second chemical compound to the polypeptide in the presence of the chemical compound indicating that the chemical compound binds to the polypeptide.

113. The process of claim 112, wherein the polypeptide has the amino acid sequence shown in Figure 5 (Seq. I.D. No. 10).

114. The process of claim 112, wherein the cell is an insect cell.

115. The process of claim 112, wherein the cell is a mammalian cell.

116. The process of claim 115, wherein the cell is nonneuronal in origin.

117. The process of claim 116, wherein the nonneuronal cell is a COS-7 cell, a 293 human embryonic kidney cell, an NIH-3T3 cell or an LM(tk-) cell.

118. The process of claim 112, wherein the compound is not previously known to bind to the polypeptide.

09116676, 071698

119. A compound determined by the process of claim 112.

120. A pharmaceutical composition which comprises an effective amount of a compound determined by the process of claim 112 and a pharmaceutically acceptable carrier.

121. A method of screening a plurality of chemical compounds not known to bind to a polypeptide encoded by a nucleic acid of claim 8 or 9 to identify a compound which specifically binds to the polypeptide, which comprises:

(a) contacting cells transfected with and expressing DNA encoding the polypeptide with a compound known to bind specifically to the polypeptide;

(b) contacting the preparation of step (a) with the plurality of compounds not known to bind specifically to the polypeptide, under conditions permitting binding of compounds known to bind the polypeptide;

(c) determining whether the binding of the compound known to bind to the polypeptide is reduced in the presence of the plurality of compounds, relative to the binding of the compound in the absence of the plurality of compounds; and if so

(d) separately determining the binding to the polypeptide of each compound included in the plurality of compounds, so as to thereby identify the compound which specifically binds to the polypeptide.

09116676.071698

122. The method of claim 121, wherein the cell is a mammalian cell.

123. The method of claim 122, wherein the mammalian cell is non-neuronal in origin.

124. The method of claim 123 wherein the non-neuronal cell is a COS-7 cell, a 293 human embryonic kidney cell, an LM(tk-) cell or an NIH-3T3 cell.

125. A pharmaceutical composition comprising an effective amount of a compound identified by the method of claim 121 and a pharmaceutically acceptable carrier.

126. A method of screening a plurality of chemical compounds not known to bind to a polypeptide of claim 10 to identify a compound which specifically binds to the polypeptide, which comprises:

(a) preparing a cell extract or cell supernatant from cells transfected with and expressing DNA encoding the polypeptide and contacting the cell extract or cell supernatant with a compound known to bind specifically to the polypeptide;

(b) contacting the preparation of step (a) with the plurality of compounds not known to bind specifically to the polypeptide, under conditions permitting binding of compounds known to bind the polypeptide;

(c) determining whether the binding of the compound known to bind to the polypeptide is reduced in the presence of the compounds, relative to the binding of the compound in the absence of the plurality of compounds; and if so

09116676.071698

(d) separately determining the binding to the polypeptide of each compound included in the plurality of compounds, so as to thereby identify the compound which specifically binds to the polypeptide.

5

127. The method of claim 126, wherein the cell is a mammalian cell.

10

128. The method of claim 127, wherein the mammalian cell is non-neuronal in origin.

15

129. The method of claim 128 wherein the non-neuronal cell is a COS-7 cell, a 293 human embryonic kidney cell, an LM(tk-) cell or an NIH-3T3 cell.

20

130. A pharmaceutical composition comprising an effective amount of a compound identified by the method of claim 126 and a pharmaceutically acceptable carrier.

25

131. A process for determining whether a chemical compound is an Ob receptor agonist which comprises contacting cells transfected with and expressing DNA of claim 9 with the compound under conditions permitting the activation of the Ob receptor, and detecting an increase in Ob receptor activity, so as to thereby determine whether the compound is an Ob receptor agonist.

30

132. A process for determining whether a chemical compound is an Ob receptor agonist which comprises preparing a cell extract from cells transfected with and expressing DNA of claim 9, isolating a membrane fraction from the cell extract, contacting the membrane fraction with the compound under conditions permitting the activation of the Ob receptor, and

35

09116676.071698

detecting an increase in Ob receptor activity, so as to thereby determine whether the compound is an Ob receptor agonist.

5 133. A process for determining whether a chemical
compound is an Ob receptor antagonist which
comprises contacting cells transfected with and
expressing DNA of claim 9 with the compound in the
presence of a known Ob receptor agonist, under
10 conditions permitting the activation of an Ob
receptor, and detecting a decrease in Ob receptor
activity, so as to thereby determine whether the
compound is an Ob receptor antagonist.

15 134. A process for determining whether a chemical
compound is an Ob receptor antagonist which
comprises preparing a cell extract from cells
transfected with and expressing DNA of claim 9,
isolating a membrane fraction from the cell extract,
20 contacting the membrane fraction with the ligand in
the presence of a known Ob receptor agonist, under
conditions permitting the activation of the Ob
receptor, and detecting a decrease in Ob receptor
activity, so as to thereby determine whether the
25 compound is an Ob receptor antagonist.

135. The process of any one of claims 131, 132, 133, or
134, wherein the Ob receptor is a mammalian Ob
receptor.

30 136. The process of any one of claims 131, 132, 133, or
134, wherein the cell is an insect cell.

137. The process of any one of claims 131, 132, 133, or
35 134, wherein the cell is a mammalian cell.

09116676.071698

138. The process of claim 137, wherein the cell is nonneuronal in origin.

139. The process of claim 138, wherein the nonneuronal cell is a COS-7 cell, a 293 human embryonic kidney cell, an NIH-3T3 cell or an LM(tk-) cell.

140. A pharmaceutical composition comprising an effective amount of a polypeptide of claim 10 and a pharmaceutically acceptable carrier.

141. The pharmaceutical composition of claim 140, wherein the pharmaceutical composition is a liquid.

142. The pharmaceutical composition of claim 141, wherein the carrier is isotonic saline.

143. A method for determining whether a compound modulates leptin activity which comprises:

(a) administering to an animal a polypeptide of claim 10 and measuring the amount of food intake, metabolic, or body weight changes in the animal;

(b) administering to a second animal both the polypeptide and the compound, and measuring the amount of food intake, metabolic, or body weight changes in the second animal; and

(c) determining whether the amount of food intake, metabolic, or body weight change is altered in the presence of the compound relative to the amount of food intake, metabolic, or body weight change in the absence of the compound, so as to thereby determine whether the compound modulates leptin activity.

09116676-071698

144. A method of screening a plurality of compounds to identify a compound which modulates leptin activity which comprises:

5 (a) administering to an animal a polypeptide of claim 10 and measuring the amount of food intake, metabolic, or body weight changes in the animal;

10 (b) administering to a second animal the polypeptide and at least one compound of the plurality of compounds and measuring the amount of food intake, metabolic, or body weight changes in the animal;

15 (c) determining whether the amount of food intake, metabolic, or body weight change is altered in the presence of at least one compound of the plurality relative to the amount of food intake, metabolic, or body weight change in the absence of at least one compound of the plurality, and if so;

20 (d) separately determining whether each compound modulates leptin activity according to the method of claim 143, so as to thereby identify a compound which modulates leptin activity.

25 145. A method of treating an abnormality in a subject, wherein the abnormality is alleviated by modulating the activity of leptin in the subject, which comprises administering to a subject an amount of the pharmaceutical composition of claim 140 effective to modulate the activity of leptin in the subject, thereby treating the abnormality in the subject.

30

35

09116676-071698

146. The method of claim 145, wherein the pharmaceutical composition is administered with food.
147. The method of claim 145, wherein the subject is a vertebrate, a mammal, a human, a canine or a feline.
148. A method of claims 145, wherein the pharmaceutical composition comprises an injectable carrier.
149. The method of claim 145, wherein the pharmaceutical composition comprises a wild-type polypeptide.
150. A method of modulating feeding behavior or metabolism of a subject which comprises administering to the subject an amount of a polypeptide of claim 10 effective to modulate the feeding behavior or metabolism of the subject so as to thereby modulate feeding behavior or metabolism of the subject.
151. The method of claim 150, wherein the subject's anorexia is treated.
152. The method of claim 150, wherein the subject's weight loss associated with cancer is treated.
153. The method of claim 150, wherein the subject's reduced appetite associated with aging is treated.
154. The method of claim 150, wherein the subject's obesity is treated.
155. The method of claim 150, wherein the subject's bulimia is treated.
156. The method of claim 150, wherein the compound is administered with food.

09416676-071698

157. The method of claim 150, wherein the subject is a vertebrate, a mammal, a human, a canine or a feline.

158. A method of claim 150, wherein the polypeptide is administered in a pharmaceutical composition comprising an injectable carrier.

159. The method of claim 150, wherein the polypeptide is a wild-type polypeptide.

160. A method of modulating feeding behavior or metabolism of a subject which comprises administering a polypeptide of claim 10 and a compound which binds to the Y5 receptor, the amount of such polypeptide and compound being effective to modulate the feeding behavior or metabolism of the subject.

161. The method of claim 160, wherein the polypeptide and the compound are administered in combination.

162. The method of claim 160, wherein the polypeptide and the compound are administered separately.

163. The method of claim 160, wherein the polypeptide and the compound are administered once.

164. The method of claim 160, wherein the polypeptide and the compound are administered alternately.

165. The method of claim 160, wherein the polypeptide and the compound are administered repeatedly.

166. The method of claim 160, wherein the polypeptide and compound are administered with food.

167. The method of claim 160, wherein the subject is a

09116676.071698

vertebrate, a mammal, a human, a canine or a feline.

5 168. A method of claim 160, wherein the polypeptide and compound are administered in a pharmaceutical composition comprising an injectable carrier.

169. The method of claim 160, wherein the polypeptide is a wild-type polypeptide.

10 170. A method of modulating feeding behavior or metabolism in a subject which comprises administering to the subject an amount of a compound which binds to a polypeptide of claim 10 effective to alter the activity of leptin in the subject, so
15 as to thereby modulate feeding behavior or metabolism of the subject.

171. The method of claim 170, wherein the subject's anorexia is treated.

20 172. The method of claim 170, wherein the subject's weight loss associated with cancer is treated.

25 173. The method of claim 170, wherein subject's reduced appetite associated with aging is treated.

174. The method of claim 170, wherein the subject's obesity is treated.

30 175. The method of claim 170, wherein the subject's bulimia is treated.

176. The method of claim 170, wherein the compound is administered with food.

35 177. The method of claim 170, wherein the subject is a vertebrate, a mammal, a human, a canine or a feline.

09116676.071608

178. A method of claim 170, wherein the compound is administered in a pharmaceutical composition comprising an injectable carrier.
- 5 179. The method of claim 170, wherein the polypeptide is a wild-type polypeptide.
- 10 180. A method of modulating feeding behavior or metabolism of a subject which comprises administering a compound which binds to a polypeptide of claim 10 and a second compound which binds to the Y5 receptor, the amount of the first compound and the second compound being effective to modulate the feeding behavior or metabolism of the subject.
- 15 181. The method of claim 180, wherein the compound and the second compound are administered in combination.
- 20 182. The method of claim 180, wherein the compound and the second compound are administered separately.
183. The method of claim 180, wherein the compound and the second compound are administered once.
- 25 184. The method of claim 180, wherein the compound and the second compound are administered alternately.
185. The method of claim 180, wherein the compound and the second compound are administered repeatedly.
- 30 186. The method of claim 180, wherein the compound and second compound are administered with food.
- 35 187. The method of claim 180, wherein the subject is a vertebrate, a mammal, a human, a canine or a feline.

00116676.071698

188. A method of claim 180, wherein the compound and second compound are administered in a pharmaceutical composition comprising an injectable carrier.

5

189. The method of claim 180, wherein the polypeptide is a wild-type polypeptide.

10

190. A method of detecting expression of a polypeptide of claim 10 by detecting the presence of mRNA coding for the polypeptide which comprises obtaining total mRNA from the cell and contacting the mRNA so obtained with the nucleic acid probe of claim 49 under hybridizing conditions, detecting the presence of mRNA hybridized to the probe, and thereby detecting the expression of the polypeptide by the cell.

15

20

191. A method of detecting the presence of a polypeptide which comprises contacting the cell or cell supernatant with the antibody of claim 56 under conditions permitting binding of the antibody to the polypeptide, detecting the presence of the antibody bound to the cell or cell supernatant, and thereby detecting the presence of a polypeptide.

25

30

192. A method of determining the physiological effects of varying levels of activity of polypeptides which comprises producing a transgenic nonhuman mammal of claim 65 whose levels of polypeptide activity are varied by use of an inducible promoter which regulates polypeptide expression.

35

193. A method of determining the physiological effects of varying levels of activity of polypeptides which comprises producing a panel of transgenic nonhuman mammals of claim 65 each expressing a different

09116676.071698

amount of polypeptide.

194. A method for diagnosing a predisposition to a disorder associated with the activity of a specific polypeptide allele which comprises:

- (a) obtaining DNA of subjects suffering from the disorder;
- (b) performing a restriction digest of the DNA with a panel of restriction enzymes;
- (c) electrophoretically separating the resulting DNA fragments on a sizing gel;
- (d) contacting the resulting gel with a nucleic acid probe capable of specifically hybridizing with a unique sequence included within the sequence of a nucleic acid molecule encoding a polypeptide and labeled with a detectable marker;
- (e) detecting labeled bands which have hybridized to the nucleic acid of claim 1 labeled with a detectable marker to create a unique band pattern specific to the DNA of subjects suffering from the disorder;
- (f) preparing DNA obtained for diagnosis by steps a-e; and
- (g) comparing the unique band pattern specific to the DNA of subjects suffering from the disorder from step e and the DNA obtained for diagnosis from step f to determine whether the patterns are the same or different and to diagnose thereby predisposition to the disorder if the

09116676-071698

patterns are the same.

5 195. The method of claim 194 wherein the disorder associated with the activity of a specific polypeptide allele is diagnosed.

196. A method of preparing the purified polypeptide of claim 10 which comprises:

10 (a) inducing cells to express the polypeptide;

(b) recovering the polypeptide from the induced cells; and

15 (c) purifying the polypeptide so recovered.

197. The method of claim 196, wherein the cell is placed in a serum-free growth medium.

20 198. The method of claim 196, wherein the polypeptide is recovered by affinity chromatography.

199. The method of claim 196, wherein the affinity chromatography comprises the use of leptin.

25 200. The method of claim 196, wherein the polypeptide is recovered by means of antibody binding.

30 201. The method of claim 200, wherein the antibody is directed to a flag epitope modification of the wild-type polypeptide.

202. A method of preparing the purified polypeptide of claim 10 which comprises:

35 (a) inserting nucleic acid encoding the polypeptide in a suitable vector;

09116576.071698

(b) introducing the resulting vector in a suitable host cell;

(c) placing the resulting cell in suitable condition permitting the production of the isolated polypeptide;

(d) recovering the polypeptide produced by the resulting cell; and

(e) purifying the polypeptide so recovered.

203. The method of claim 202, wherein the cell is placed in a serum-free growth medium.

204. The method of claim 202, wherein the polypeptide is recovered by affinity chromatography.

205. The method of claim 202, wherein the affinity chromatography comprises the use of leptin.

206. The method of claim 202, wherein the polypeptide is recovered by means of antibody binding.

207. The method of claim 206, wherein the antibody is directed to a flag epitope modification of the wild-type polypeptide.

add B2 > add C'

09116676-071698